REMARKS

Reconsideration of the above-identified application in view of the remarks following is respectfully requested.

In a telephone interview graciously granted by the Examiner, Applicant proposed to amend claim 1 to limit the claim to a plurality of MHC-peptide complexes which are all recognizable by one CTL clone.

In said interview, the Examiner acknowledged that the MHC-peptide complexes taught by the prior art consist of a heterogeneous population of complexes which are recognized by several CTL clones. In contrast, the MHC-peptide complexes formed according to the teachings of the instant application consist of a homogenous population of complexes which are all recognized by one CTL clone.

Claims 1-13 are in this case. Claims 4-11 were Withdrawn under a restriction requirement as drawn to a non-elected invention. Claim 3 has been canceled. Claims 1, 2, 12 and 13 have been rejected. Claims 1, 2, 12 and 13 have now been amended. Claims 14-17 have now been added.

35 U.S.C. §103(a) Mottez in view of Lone

The Examiner has rejected claims 1 and 2 under 35 U.S.C. 103(a) as being unpatentable over Mottez et al (J. Exp. Med. 1995, 181: 493-502) in view of Lone et al., (J. Immunotherapy, 1998, 21:283-294). The Examiner's states that Mottez teaches single constructs comprising a murine MHC class I heavy chain joined to β2-microglobulin with a covalently bound antigenic peptide. In addition, the Examiner states that Lone et al., teaches that the same techniques were applied to human MHC class I heavy chain HLA-A2.1, which was joined via a 15-amino acid linker to human β2-microglobulin. The Examiner further states that Lone teaches that the single chain MHC class I construct specifically bound HLA-A2 restricted peptides and induced peptide-specific cytotoxic T cells to proliferate and produce IL-2. The Examiner's rejections are respectfully traversed. Claim 1 has now been amended. New claims 14-17 have now been added.

Applicant points out that the MHC class I complexes taught by Motezz and Lone are derived from eukaryotic cells and therefore inherently consist of some of the endogenous peptide and/or MHC heavy chain and/or β2 microglobulin left

following the peptide stripping process along with the recombinant polypeptides. Due to their heterologous source, various combinations of complexes can be formed, resulting in a plurality of heterogeneous complexes which are recognizable by several different CTL clones and not by one CTL clone. In addition, due to the instable configuration of the MHC-peptide complexes formed according to the prior art teachings (Lone et al.), binding assays to CTL clones were performed on dimerized peptide/SC-A2 complexes which were obtained using the anti-β2M mAB (FMC16mAb) (see Lone et al. Page 285, right column lines 3-8; Page 287, left column lines 26-30; and Page 288, description of Figure 3).

In sharp contrast to the cited prior art, the MHC-I-peptide complexes of the present invention are obtained by recombinant expression in prokaryotic cells which lack the endogenous MHC-I polypeptides and/or the proteasome system and thus consist of only the recombinant and/or synthetic polypeptides. Thus, the present invention discloses, for the first time, a homogenous population of MHC-I-peptide complexes which are all recognizable by one CTL clone.

To better distinguish the claimed invention from the prior art, Applicant has elected to amend claim 1 to recite:

> *"1. A plurality of complexes each being composed of an antigenic peptide being capable of binding a human MHC class I, and a chimeric polypeptide which comprises a functional human β-2 microglobulin translationally fused to a functional human MHC class I heavy chain, wherein all of the plurality of complexes are recognizable by one CTL clone."*
>
> (Emphasis added)

Support for the claim language can be found on Page 51, lines 19-23 and Page 52, lines 1-3 of the instant application.

In addition, in contrast to the MHC-peptide dimers used for CTL activation in Lone et al., the plurality of MHC-I-peptide complexes of the instant application constitute a uniform and homogenous monomeric population of molecules (see Figures 3a-b and in Page 46, lines 16-23 and Page 47, lines 1-13 of the instant application) which can be used for therapeutic purposes without triggering several and undesired CTL clones.

Thus, Applicant has elected to add new claims 14-17 which clearly distinguishe the MHC-peptide monomeric complexes of the instant application from the MHC-peptide dimers taught by the prior art.

New claim 14 now recites:

"14. The plurality of complexes of claim 1, wherein each of said plurality of complexes is a monomeric complex."
(Emphasis added)

Support for the claim language can be found in Page 46, line 19 and Page 47, lines 1-13 of the instant application.

Thus, the instant application presents, for the first time, a plurality of MHC-peptide monomeric complexes each composed of an antigenic peptide being capable of binding a human MHC class I and a chimeric polypeptide which comprises a functional human β2-microglobulin translationally fused to a functional human MHC class I heavy chain. The homogenous population of monomeric complexes disclosed by the instant application is advantageous over the MHC-peptide dimers taught by the prior art since it can be used, for example, as an immunogen for generating antibodies with CTL-like specificity, *i.e.*, which are capable of recognizing monomers of specific MHC-peptide complexes as naturally exist in the human body.

In view of the claim amendments, claim additions and accompanying arguments, Applicant believes that the present invention as now claimed in claims 1, 2, 12, 13 and new claims 14-17 is novel and non-obvious.

35 U.S.C. §112, first paragraph

The Examiner has rejected claims 1, 2, 12 and 13 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Specifically, the Examiner states that claim 1 and new claim 13 recites "biologically functional β2M" and "biologically functional human MHC class I heavy chain", however, review of the specification and claims as originally filed shows numerous recitations of "functional β2M" and "functional human MHC class

I heavy chain", but no recitation of "biologically functional". In addition, the Examiner states that while the specification defines the term "functional" at Page 22, lines 3-8, the definition does not address the term "biological functional".

In addition, the Examiner states that claims 1, 2 and 12 were amended to recite a "composition comprising a plurality of complexes... wherein said plurality of complexes are recognizable by a single specific CTL clone", however the recited limitation is not supported by the specification or claims as originally filed. Specifically, the Examiner states that the specification discloses the making of an MHC class I complex and the use of that complex to present specific antigenic CTL clones, for example at page 19, lines 15-17, but the specification does not discloses a "composition" of such complexes that present antigenic peptide to a "single" specific CTL clone.

Applicant has elected to amend claims 1, 2, 12 and 13 to remove the terms "biologically", "composition" and "single" from the claims, thereby rendering moot the Examiner's rejections.

In view of the claim amendments, Applicant believes to have overcome the U.S.C. §112, first paragraph rejections with respect to claims 1, 2, 12 and 13.

35 U.S.C. §112, second paragraph

The Examiner rejected claims 1, 2, 12 and 13 under U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that claims 1, 2 and 13 are each ambiguous and unclear in the recitation of "biological functional" and that the term is not disclosed or defined in the specification, so it is unclear what type of biological functions are exhibited by the complex recited in the claims.

As mentioned hereinabove, the Examiner found that the term "functional" is well defined by the specification (Page 22, lines 3-8) with respect to binding and presenting to CTL specific antigenic peptide when complexed. As mentioned hereinabove, Applicant has removed the term "biologically" from claims 1, 2 and 13, thus rendering moot the Examiner's rejection.

In view of the claim amendments, Applicant believes to have overcome the U.S.C. §112, second paragraph rejections with respect to claims 1, 2 and 13.

In view of the above amendments and remarks it is respectfully submitted that claims 1-2, 12-17 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

Martin D. Moynihan

Martin D. Moynihan
Registration No. 40,338

Date: July 17, 2006

Enclosed:
Petition for Extension (1 Month); and
Request for Continued Examination (RCE)